REMARKS

Claims 24, 26, 27, 29, and 37-39 are pending in the application.

Applicants respectfully request reconsideration and allowance of claims 24, 26, 27, 29, and 37-39 in view of the above amendments and following remarks.

Regarding 35 U.S.C. §112, second paragraph

The Office continues to reject claim 38 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite with respect to the phrase "highly stringent" hybridization conditions. The Office asserts that claim 38 does not define the stringent hybridization conditions that include "hybridization at 60C in a solution with a sodium ion concentration from about 0.01 to 1.0M, pH 7.0 to 8.3 comprising formamide" and cited to page 11 of the specification. The Office suggests amending the claims by "distinctly defining the conditions, including washing conditions, under which highly stringent conditions are practiced." Applicants again respectfully disagree.

The Court of Appeals for the Federal Circuit has held and repeatedly affirmed that definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. See, e.g., In *re Marosi*, 710 F.2d 799, 218 U.S.P.Q. 289 (Fed. Cir. 1983); *Rosemount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 221 U.S.P.Q. 1 (Fed. Cir. 1984); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983); and *Atmel Corp. v. Information Storage Devices, Inc.*, 198 F.3d 1374, 53 U.S.P.Q.2d 1225 (Fed. Cir. 1999) (district court failed to consider the knowledge of one skilled in the art when interpreting the patent disclosure).

Claims are not indefinite merely because they present a difficult task of claim construction. *Halliburton Energy Services, Inc. v. M-I LLC 2007-1149* Instead, "[i]f the meaning of the claim is discernible, even though the task may be formidable and the conclusion may be one over which reasonable persons will disagree, we have held the claim sufficiently clear to avoid invalidity on indefiniteness grounds." *Halliburton Energy Services, Inc. v. M-I LLC 2007-*

1149 (quoting Exxon Research & Eng'g Co. v. United States, 265 F.3d 1371, 1375 (Fed. Cir. 2001)) (citations omitted). "Only claims 'not amenable to construction' or 'insolubly ambiguous' are indefinite." *Datamize v. Plumtree Software, Inc.*, 417 F.3d 1342, 1347 (Fed.Cir.2005) (citing *Novo Indus., L.P. v. Micro Molds Corp.*, 350 F.3d 1348, 1353 (Fed. Cir. 2003); *Honeywell International, Inc. v. International Trade Commission*, 341 F.3d 1332, 1338 (Fed. Cir. 2003); *Research & Eng'g Co. v. United States*, 265 F.3d at 1375 (Fed.Cir.2001))

Claim 38 recites high stringency hybridization conditions. The Office is reminded that Furthermore, as high stringency conditions are known in the art, one of ordinary skill in the art could readily determine suitable washing conditions. Furthermore, the specification teaches appropriate washing conditions, for example, at paragraph [0055]. Applicants submit that claim 38 is sufficiently definite under the controlling legal standards set forth above. In other words, claim 38 is not indefinite in light of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. Accordingly, the Office is respectfully requested to withdraw the rejection of claim 38 under 35 U.S.C. §112, second paragraph.

Regarding 35 U.S.C. §112, First Paragraph (Enablement)

The Office again rejects claims 24, 26, 27, and 37-39 under 35 U.S.C. §112, first paragraph, for an alleged lack of enablement. Applicant respectfully maintains that the specification enables the full scope of the claimed invention for the reasons that follow.

In *Amgen, Inc. v. Hoechst Marion Roussel, Inc*, 232 F.3d 905 (Fed.Cir. 2000), the Federal Circuit clarified the enablement requirement:

> The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without "undue experimentation."

Id. (citing *Genentech, Inc. v. Novo Nordisk, A/S,* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991))

In *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 47 U.S.P.Q.2d 1705 (Fed. Cir. 1998), the Federal Circuit clearly stated that routine experimentation does not constitute undue experimentation:

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Id. (Emphasis added) (citing *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d at 1564, 37 U.S.P.Q.2d at 1623); see also *In re Wands*, 858 F.2d at 736-40, 8 U.S.P.Q.2d at 1403-07.

The claimed methods do not relate to hundreds of CA nucleic acids. Rather, the claims relate to nucleic acids having a particular sequence, SEQ ID NO:167 or the full complement thereof, and nucleic acids at least 98% identical to the nucleotide sequence set forth in SEQ ID NO:167. Furthermore, the claims recite that patients are diagnosed with colon cancer when a decrease in the level of the recited nucleic acid is observed relative to the control.

The Office relies on Tockman *et al.* (*Cancer Research*, 1992) to support the alleged lack of enablement. The Tockman *et al.* reference discusses the steps recommended for bringing a biomarker into clinical application, a commercial application of a biomarker. As stated in MPEP § 2164, in order to comply with 35 U.S.C. §112, first paragraph, "it is not necessary to 'enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim to that effect.' *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003) ..." Thus, the teachings of Tockman *et al.* are not relevant when considering whether an invention is enabled under 35 U.S.C. §112, first paragraph. Applicant submits that the standard for enablement is not a "certainty" of success, but a "reasonable expectation" of success, and that a "conclusive determination" or "irrefutable" demonstration of diagnostic efficacy is not required for patentability. The courts have consistently held that this is not the proper level of inquiry when assessing utility and enablement under Title 35. The proper standard for enablement is that the specification teaches those of ordinary skill in the art how to make and use the invention without "undue experimentation." MPEP 2164.01. Further, at no point does the Tockman *et al.* reference suggest that a biomarker that has not yet been validated for use in the clinic is not suitable as a biomarker in general. Thus, the Tockman *et al.* reference provides guidelines for validating biomarkers for commercial

clinical use, but it is not relevant or instructive for evaluating whether the presently claimed invention is enabled under 35 U.S.C. § 112, first paragraph.

The Office refutes the above arguments by arguing the Applicants are not claiming a "general biomarker," but rather claim methods of using the biomarker to diagnose a particular disease. Office Action mailed 2/26/09 at page 10. The Office misunderstands Applicants argument, which is simply that only because a biomarker has not been validated for clinical use to diagnose a particular disease, does not mean it is not enabled to diagnose the particular disease. Furthermore, the Office organized its enablement analysis around the Wands factors. *In re Wands, 858 F.2d 731, 736-37 (Fed. Cir. 1988).* The Office is reminded that the *Wands* factors are "**illustrative**, not mandatory," *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991).

Applicants respectfully assert that the specification enables one of ordinary skill in the art to practice the methods of claims 24, 26, 27, and 37-39 without undue experimentation. One of ordinary skill in the art can readily determine if expression of a nucleic acid having the nucleotide sequence set forth in SEQ ID NO:167, or a nucleic acid having at least 98% identity to SEQ ID NO:167, is decreased relative to that of a control sample. One of ordinary skill in the art also can readily determine if the amount of duplex formed upon contacting a polynucleotide that hybridizes under highly stringent conditions to a nucleic acid having the nucleotide sequence set forth in SEQ ID NO:167 or full complement thereof with a patient sample is decreased relative to the amount of duplex formed by hybridization of such a polynucleotide to a control non-cancer sample (see claim 38). The specification provides detailed guidance for detecting mRNA, e.g., at paragraphs [128] - [0133] of the specification, and for hybridization, e.g., at paragraphs [0055] and [0133] of the specification. One of ordinary skill in the art will appreciate that decreased expression of EGR1 mRNA can be used to facilitate diagnosis of colon cancer.

In view of the above, Applicants assert that the specification enables one of ordinary skill in the art to practice the methods of claims 24, 26, 27, and 37-39. The Office is requested to withdraw the rejection under 35 U.S.C. §112, first paragraph, for lack of enablement.

Regarding 35 U.S.C. §112, First Paragraph (New Matter)

Applicants respectfully traverse the rejection of claims 24, 26, 27, and 37-39 under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, had possession of the claimed invention at the time the application was filed.

The Office asserts that the specification discloses that SEQ ID NO:167 is a cancer associated (CA) nucleic acid and further discloses that CA nucleic acids can be downregulated or upregulated in carcinomas. The Office alleges that, of the hundreds of CA nucleic acids disclosed in the specification (see Table 1), the specification does not disclose which CA nucleic acids are uprequlated and which are downregulated in a particular carcinomas.

Rewording, making inherent function explicit, making explicit material incorporated by reference not new matter. The specification provides written description for both upregulation and downregulation of SEQ ID NO: 167. When a disclosure describes a claimed invention in a manner that permits one skilled in the art to reasonably conclude that the inventor possessed the claimed invention the written description requirement is satisfied. (MPEP §2163 (emphasis added)). This possession may be shown in any number of ways and an Applicant need not describe every claim feature exactly because there is no *in haec verba* requirement. (MPEP § 2163) *Application of Edwards*, 568 F.2d 1349, 1351-52 (C.C.P.A. 1978); *see also Crown Operations Int'l, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1376, (Fed.Cir. 2002) ("the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue"); *New Railhead Mfg. L.L.C. v. Vermeer Mfg. Co.*, 298 F.3d 1290, 1296 (Fed. Cir. 2002) ("[i]dentity of description is not necessary"). Rather, to satisfy the written description requirement, all that is required is "reasonable clarity." (MPEP § 2163.02). Also, an adequate description may be made in any way through express, implicit, or even inherent disclosures in the application, including words, structures, figures, diagrams, and/or formulae. (MPEP §§ 2163(I), 2163.02). Finally, it is important to be mindful of the generally inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. (MPEP § 2163(II)(A)(2)) (inventions in "predictable" or "mature" require a lesser showing of possession than inventions in more "unpredictable" arts).

Application of Edwards, 568 F.2d 1349, 1351-52 (C.C.P.A. 1978); *see also Crown Operations Int'l, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1376, (Fed.Cir. 2002) ("the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue"); *New Railhead Mfg. L.L.C. v. Vermeer Mfg. Co.*, 298 F.3d 1290, 1296 (Fed. Cir. 2002) ("[i]dentity of description is not necessary").

Further, the Office argues that the specification *lacks working examples* demonstrating methods wherein a decrease of at least 50% in a level of expression of a nucleic acid in a patient sample as compared to a second sample indicates the patient has colon cancer. The lack of a working example is not relevant to the issue of new matter.

Applicants respectfully submit that each of the claim elements is taught as it relates to the CA nucleic acids, including SEQ ID NO: 167 in the specification as previously set forth on the record. Applicants respectfully request removal of the rejection of claims 24, 26, 27, and 37-39 under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, had possession of the claimed invention at the time the application was filed.

CONCLUSION

In light of the remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned attorney if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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